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The etiology, biology, and evolving pathology of premenstrual syndromes.

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Menstrually related symptoms and disorders are multidimensional and affect diverse physiologic systems. Elucidation of the pathophysiologic mechanisms of these disorders should allow for a more precise diagnosis, and provide direction for targeted therapeutic interventions. Several biologic mechanisms that underlie menstrually related symptoms have been proposed. They focus mostly on gonadal hormones, their metabolites and interactions with neurotransmitters and neurohormonal systems, such as serotonin, GABA, cholecystokinin, and the renin-angiotensin-aldosterone system. Altered responses of these systems to gonadal hormone's fluctuations during the menstrual cycle, as well as an increased sensitivity to changes in gonadal hormones may contribute to menstrually related symptoms in vulnerable women. Disrupted homeostasis and deficient adaptation may be core underlying mechanisms. Future directions for clinically-relevant progress include identification of specific subgroups of menstrually-related syndromes, assessment of the genetic vulnerability and changes in vulnerability along the life cycle, the diversified mechanisms by which vulnerability is translated into pathophysiology and symptoms, the normalization process as well as syndromes-based and etiology-based clinical trials.